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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/688,142	10/17/2003	William J. Curatolo	PC10805B	9233

28523 7590 02/09/2005

PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
BERKO, RETFORD O	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/688,142	CURATOLO ET AL.	
	Examiner	Art Unit	
	Retford Berko	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement: The Information Disclosure Statement filed on November 8, 2004 is acknowledged.

Status of Claims

Claims 1-75 are on file and pending review.

Joint Inventors

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-46 are rejected as unpatentable under 35 U.S.C. 103(a) over Myers et al (US 5, 891, 845) in view of the combination of Benet et al (US 6, 004, 927) and Curatolo et al (US 5, 605, 889).

Independent claim 1 is drawn toward a method for increasing the bioavailability of azithromycin comprising co-administration of azithromycin and a glycoprotein inhibitor (gp-inhibitor). According to dependent claims, the glycoproten inhibitor is antimicrobially effective and the method entails different routs of administration (e.g. oral or intravenous); resulting in increased bioavailability during treatment.

According to applicant, verapamil is a known P-glycoprotein inhibitor (specifiction at page 19, lin 1-10). It is also generally known in the art that other P-glycoprotein inhibitors include compounds such as cyclosporin, S9788, MK571 and stable S-substituted derivatives of glutathione (e.g. dinitrophenacyl glutathione); while azithromycin and compounds such as erythromycin, clarithromycin and leocomycin are effective class of antibiotics known as macrolides.

Myers et al (Patent '845) disclose controlled release drug delivery formulations comprising cyclosporin and said composition having advantage of eliminating large blood level fluctuations when patient is taking other drugs (col 16, lin 10-19). According to Myers, verapamil; antifungals (e.g. fluconazole) and antibiotics (e.g. erythromycin) —both compounds are gp-inhibitors enhances the blood levels of cyclosporin (col 16, lin 10).

Patent '845 does not disclose co-administration of a gp-inhibitor with azithromycin.

Benet et al (Patent '927) discloses a method for increasing bioavailability of orally administered drugs to patients wheren a drug is concurrently administered with a bioenhancer that is an inhibitor of gp-glycoprotein (abstract, and col 25, lin 20-40). Though Benet et al do not disclose the coadministration of azithromycin with a pg-inhibitor, according to Benet,. ketonazole when used in combination with certain drugs increases the bioavailability of active compounds in a drug composition e.g. enhancing the cyclosporin levels (col 21, lin 30, col 22, lin 40-60 and col 25, lin 20-40).

Curatolo et al (Patent '889) is relied upon for the disclosure dosage forms of azithromycin and a method of administering azitromycin to patients (abstract, col 6, lin 55 and col 22, lin 25-40).

One of ordinary skill in the art would be motivated to administer a drug composition comprising a gp-inhibitor comprising azithromycin (a macrolide) and a gp-inhibitor (e.g. verapamil). The method of replacing azithromycin with another macrolide (ketonazole or erythromycin) on one hand is within the level of experience of one of ordinary skill in the art because as shown in the prior at cited, one of ordinary skill would expect that co-administration of the compounds (antimicrobial agent and gp-inhibitor) would reasonably lead to increase in the bioavailability of the active agent (Patent '927, col 22, lin 35-60 and col 25, lin 20-40) as well as eliminate large fluctuations of drug and thereby provide steady levels of active compound for effective therapy (Patent '845, col 16, lin 15-20). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

Claims 1 and 49-75 are rejected as unpatentable under 35 U.S.C. 103(a) over Curatolo et al (US 5, 605, 889) in view of Chhabra et al (US 6, 500, 459; filed July 21, 1999) further in view of the combination of Myers et al (US 5, 891, 845) and Benet et al (US 6, 004, 927).

Independent claim 1 is drawn toward a method for increasing the bioavailability of azithromycin comprising co-administration of azithromycin and a glycoprotein inhibitor (gp-inhibitor). According to dependent claims, the glycoproten inhibitor is antimicrobially effective and the method entails different routs of administration (e.g. oral or intravenous); resulting in increased bioavailability during treatment. The claims are further drawn toward the composition comprising azithromycin and gp-inhibitor, present to effectuate an increase in oral, blood/serum bioavailability. The claims are also drawn toward a kit comprising the composition

Curatolo et al (Patent '889) discloses azithromycin composition and a method of administering azitromycin to patients (abstract, col 6, lin 55 and col 22, lin 25-40). Patent '889 does not teach the use of gp-inhibitor in the composition.

Chhabra et al (Patent '459) discloses polymer coated, controlled release dosage forms of verapamil-Hcl (col 21, lin 55). Patent '459 does not disclose azithromycin or any other gp-inhibitor in the composition.

As discussed, Myers et al (Patent '845) disclose controlled release drug delivery formulations comprising cyclosporin and said composition having advantage of eliminating large blood level fluctuations when patient is taking other drugs (col 16, lin 10-19). Verapamil; antifungals (e.g. fluconazole) and antibiotics (e.g. erythromycin) —both compounds are gp-inhibitors.

The disclosure in Benet et al (Patent '927) was discussed above; i.e. a method for increasing bioavailability of orally administered drugs to patients wheren a drug is concurrently administered with a bioenhancer that is an inhibitor of gp-glycoprotein (abstract, and col 25, lin 20-40). Patent '927 discloses that ketonazole when used in combination with certain drugs increases the bioavailability of active compounds in a drug composition e.g. enhancing the cyclosporin levels (col 21, lin 30, col 22, lin 40-60 and col 25, lin 20-40).

One of ordinary skill in the art would be motivated to prepare a drug composition comprising a gp-inhibitor comprising azithromycin (a macrolide) and a gp-inhibitor (e.g. verapamil). One of ordinary skill would expect that co-administration of the compounds (antimicrobial agent and gp-inhibitor) would reasonably lead to increase in the bioavailability of the active agent (Patent '927, col 22, lin 35-60 and col 25, lin 20-40) as well as eliminate large fluctuations of drug and thereby provide steady levels of active compound for effective therapy (Patent '845, col 16, lin 15-20). The invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made in view of the fact that azithromycin can be replace with another macrolide (ketonazole or erythromycin and a gp inhibitor such as ketonazole or cyclosporing can be included in the composition with the reasonable expectation of obataining enhanced bioavailability of the active agents as already shown by Benet et al (Patent '927 col 25, lin 20-40).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is571-272-0590. The

examiner can normally be reached on M-F from 8.00 am to 5.30 pm. Examiner Berko has been assigned future prosecution of the application.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). RoB 1/31/05

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